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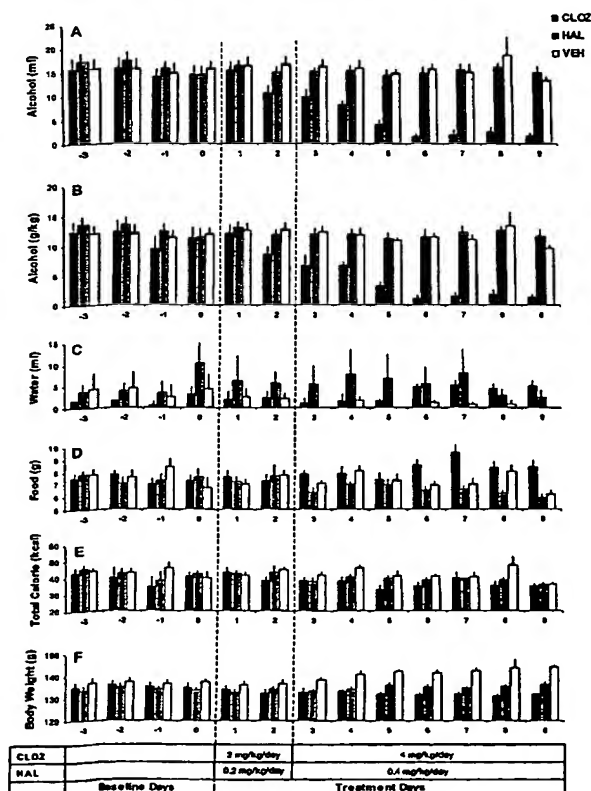
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(54) Title: TREATING ALCOHOL AND OR SUBSTANCE ABUSE BY ANTAGONIZING  $\alpha 2$  ADRENERGIC RECEPTORS WITH WEAK DOPAMINE BLOCKING



(57) Abstract: Certain atypical antipsychotic medications (particularly clozapine) or combinations of medications are useful to treat alcohol or other substance abuse, particularly in the general (non-schizophrenic) population. Generally stated, one aspect of the invention features a method of treating a patient suffering from alcohol or other substance abuse by administering to the patient medication effective to rectify an abuse-associated dysfunction in the DA-mediated brain reward circuit. A second aspect of the invention features administering medication that strongly antagonizes  $\alpha 2$  adrenergic receptors and weakly antagonizes dopamine D2 receptors. Preferably, the ratio of  $\alpha 2$  receptor blockade to D2o receptor blockade is similar to that of clozapine. The medication may be a single compound (such as clozapine or risperidone), or it may include two or more compounds which together achieve the specified function. For example, the medication may include a first component which weakly blocks the D2 receptor (such as clozapine, quetiapine or ziprasidone or a low dose of another anti-psychotic that is a more potent D2 blocker) and a second component (such as clozapine, risperidone or idazoxan) which strongly blocks  $\alpha 2$  receptors, particularly the  $\alpha 2C$  receptor. Cocktails of the two components are also disclosed.

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